

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE**

BIO-RAD LABORATORIES, INC. and THE
UNIVERSITY OF CHICAGO,

Plaintiffs,

v.

10X GENOMICS, INC.,

Defendant.

C.A. No. 15-152-RGA

**DEFENDANT 10X GENOMICS, INC.'S BENCH MEMORANDUM REGARDING
ADMISSIBILITY OF COPYING EVIDENCE**

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10X seeks to introduce evidence that substantial portions of the prior art *Quake* application¹ were copied into the provisional application to which each of the Ismagilov patents claims priority. The provisional application is relevant to the priority date of the invention. And evidence that Ismagilov copied passages from *Quake* is highly relevant to Dr. Ismagilov's credibility, as well as invalidity and damages. 10X provides this brief to address the evidence of copying and its relevance to the issues in the case.

Bio-Rad relies on the provisional application for its claimed priority date, which is Bio-Rad's burden to establish and which is relevant to enablement, anticipation, and obviousness.

Anticipation, obviousness, and enablement are measured from the perspective of a person of ordinary skill in the art at the time the invention was made. Throughout this case, Bio-Rad has maintained that its patents are entitled to a priority date of no later than May 9, 2002—based on the filing date of the provisional application. D.I. 95-1 (Plaintiffs' First Supplemental Response to Interrogatory No. 1) at 167-170; Ex. 1 (Sia Rebuttal Report), ¶ 61 ("I understand that the '091, '407, and '193 Patents claims priority to the '927 Application. The inventive concepts above from the '091, '407, and '193 Patents were originally embodied in the '927 Application.") (internal citations omitted).

10X relied on that argument in selecting and narrowing its prior art references. For example, the *Thorsen Thesis*, upon which 10X currently relies to establish the secondary consideration of simultaneous invention for invalidity, would be anticipatory prior art if Bio-Rad does not rely on the provisional application for priority. Bio-Rad is not entitled to the May 2002 priority date in the absence of the provisional application. Bio-Rad's attempt to exclude evidence of the provisional application, just days before trial, unfairly prejudices 10X.

¹ WO 02/23163 ("*Quake*").

The experts in this case also relied on that priority date in evaluating enablement, anticipation, and obviousness. For example, Professor Hsueh-Chia Chang opines that the surfactants listed in the provisional application would not stabilize droplets for off-chip reactions. *See, e.g.*, Ex. 2 (Chang Report), ¶¶ 267-69.

Further, Bio-Rad's reliance on the provisional is inconsistent with—and, accordingly, relevant to—its position that *Quake* did not disclose the “providing conditions suitable” step required by two of the Ismagilov patents. *See* D.I. 263 (Plaintiffs' Opposition to 10X's MSJ) at 28. This argument is premised on Plaintiffs' position that *Quake* does not disclose “surfactants for stabilizing biochemical reagents in a droplet.” *Id.* The jury should know that the list of “exemplary surfactants” and “preferred surfactants” disclosed in the provisional patent application were copied directly from *Quake*. *See, e.g.*, Ex. 2, ¶¶ 267-69.

The copying is relevant. Sixteen out of thirty-four pages of Ismagilov's provisional patent application contain text copied from *Quake*. *See* Ex. 3 (Ismagilov Provisional Application) at DTX-0386.0012–.0039.² These portions, copied nearly verbatim from *Quake* into the Ismagilov provisional application, cover key droplet microfluidic concepts that Bio-Rad has now attributed to the features claimed in the supposedly “foundational” Ismagilov patents, including:

- Droplet formation, including descriptions of the physical architecture of exemplary microfluidic chips for forming and analyzing droplets or plugs, including channels, droplet/plug-forming regions, and detection regions. *See, e.g.*, Ex. 3 at DTX-0386.0035-0036, Ex. 4 (*Quake*) at RI00121001 (“Preferably, the sample inlet intersects the [first/main] channel such that the pressurized sample solution is introduced into the [first/main] channel at an angle perpendicular to a stream of fluid passing through the [first/main] channel. For example, in preferred embodiments, the sample inlet and the [first/main] channel intercept at a T-shaped junction; *i.e.*, such that the sample inlet is perpendicular (90 degrees) to the [first/main] channel. However the sample inlet may intercept the [first/main] channel at any angle, and need not introduce the sample fluid to

² The material copied from *Quake* into the Ismagilov provisional largely carries over into the issued patents, with minor wording changes. *See* Ex. 5 ('407 patent).

the [first/main] channel at an angle that is perpendicular to that flow.”).³ This includes exemplary microfluidic chips with a reservoir for loading a sample, an inlet port, a “variety of channels for sample flow and mixing.” Ex. 3 at DTX-0386.0035, Ex. 4 at RI00121000. The “typical analysis unit” includes a plug-forming “region generally compris[ing] a junction between the sample inlet and the [first/main] channel” for dividing the sample into droplets/plugs separated by carrier fluids. Ex. 3 at DTX-0386.0035-0036, Ex. 4 at RI00121001.

- Conducting reactions in droplets, including using droplets as “microreactors for chemical reactions (including biochemical reactions).” Ex. 3 at DTX-0386.0016, Ex. 4 at RI00121005. This includes methods of analyzing enzymes “by the extent to which they catalyze chemical reactions of a substrate (conversely, substrate can be analyzed and/or sorted by the level of chemical reactivity catalyzed by an enzyme)” and analyzing “[c]ells and virions” “according to whether they contain or produce a particular protein.” Ex. 3 at DTX-0386.0028, Ex. 4 at RI00121009
- Surfactants, including the use of surfactants to “aid in controlling or optimizing droplet size, flow and uniformity, for example by reducing the shear force needed to extrude or inject droplets into an intersecting channel. This may affect [plug/droplet] volume and periodicity, or the rate or frequency at which [plugs/droplets] break off into an intersecting channel.”⁴ Ex. 3 at DTX-0386.0017, Ex. 4 at RI00121012. Further, the portions copied from *Quake* directly into the Ismagilov provisional application (and later, the Ismagilov patents) warn that when droplets or plugs are used as microreactors for biochemical reactions, “a water soluble surfactant such as SDS may denature or inactivate the contents of the” droplet or plug. Ex. 3 at DTX-0386.0016, Ex. 4 at RI00121005.
- Droplet detection manipulation, including sorting plugs/droplets “based on the detection or measurement of a characteristic, marker,” etc. Ex. 3 at DTX-0386.0026-0028, Ex. 4 at RI00121011-17; *see also* Ex. 3 at DTX-0386.0028, Ex. 4 at RI00121009 (“A preferred detector is an optical detector, such as a microscope, which may be coupled with a computer and/or other image processing or enhancement devices to process images or information produced by the microscope using known techniques. For example, molecules can be analyzed and/or sorted by size or molecular weight.”).

This copied material appears throughout the “Detailed Description of the Invention.”

Ex. 3 at DTX-00386.0011-0039. Indeed, “preferred embodiments” of the alleged Ismagilov

³ The Ismagilov patents refer to the channel through which the carrier fluid flows as the “first” channel, while *Quake* refers to this channel as the “main” channel. In numerous paragraphs of the Ismagilov provisional application, portions of *Quake* are copied directly into the provisional application, changing only the word “main” to the word “first.”

⁴ The Ismagilov patents use the term “plug,” while *Quake* uses the term “droplet.”

inventions are directly copied from *Quake*. See, e.g., *id* at DTX-0386.0013, 0015, 0016-0017, 0026-0027, 0028, 0029, 0030, 0032, 0034, 0035-0037 (describing “preferred embodiments” or elements of “the invention” copied from *Quake*).

Copying is relevant to Dr. Ismagilov’s credibility. Dr. Ismagilov did not attribute the copied portions of his specification to *Quake*. Instead, he signed an inventor’s oath attesting that he “believe[d]” himself to be “the original inventor or an original joint inventor of a claimed invention in the application for which the oath or declaration is being submitted.” 37 C.F.R. § 1.63(a)(3). Dr. Ismagilov is also an academic and bound by his university’s code of conduct and academic norms. Those norms require carefully crediting others’ work. Dr. Ismagilov’s statement to the Patent Office and his violation of community norms are both relevant to his credibility to the jury.

Copying is relevant to invalidity. 10X will show that the Ismagilov patents are invalid because, among other reasons, they are obvious in light of *Quake* in combination with one or more other references. According to the Supreme Court, one of the most important factors in determining obviousness is an evaluation of the “differences between the prior art and the claims at issue.” *Graham v. John Deere Co.*, 383 U.S. 1, 17 (1966). Demonstrating the extent of the copying of *Quake* into the Ismagilov provisional application (and later, into the Ismagilov patents) will aid the jury in evaluating the differences between *Quake* and the patents in suit (or lack thereof). As Prof. Chang, 10X’s invalidity expert, testified in his report, “[t]he similarities between *Quake* and [the Ismagilov patents]—which appear to be a direct result from the copying of *Quake*’s PCT application into the Ismagilov provisional application—serve to demonstrate how *Quake* anticipates or renders obvious the claims of the Ismagilov patents[.]” Ex. 2 (Chang Report), ¶ 143; see also Ex. 6 (Chart Comparing Copied Portions). Moreover, because a POSA is

presumed to have knowledge of all prior art, a POSA in this case would necessarily be aware that Ismagilov copied large portions of *Quake* into his own provisional application and patents. *See Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 963 (Fed. Cir. 1986) (“The person of ordinary skill is a hypothetical person who is presumed to be aware of all the pertinent prior art.”). To exclude this evidence of copying would improperly remove a key component of a POSA’s necessary knowledge of the prior art.

Ismagilov’s copying is also relevant to secondary considerations, another *Graham* factor. 383 U.S. at 17. As part of their “praise” arguments, Bio-Rad and its expert, Dr. Sia, have contended that the Ismagilov patents “include numerous novel elements, ***including the ability to use microfluidic droplets as compartmentalized microreactors.***” Ex. 1, ¶ 638 (emphasis added). But the Ismagilov provisional application directly copies the concept of using droplets as microreactors from *Quake*. As copied from *Quake*, the Ismagilov provisional application discloses “embodiments where aqueous [plugs/droplets] are used as ***microreactors for chemical reactions (including biochemical reactions)*** or are used to analyze and/or sort biomaterials. Ex. 3 at DTX-0386.0016 (emphasis added). This copying undermines Dr. Sia’s arguments, including his argument that “Dr. Ismagilov and his group’s inventions include numerous novel elements, the overarching novel feature being the ability to use microfluidic droplets as compartmentalized microreactors.” Ex. 1, ¶ 640. Much of Bio-Rad’s alleged “praise” evidence relates to this supposed “overarching novel feature”—which, as demonstrated by the copying from *Quake*, cannot be attributed to Ismagilov.

Copying is relevant to damages. Ismagilov’s copying is also relevant to damages. *See* Ex. 7 (Sullivan Report) at § 6.1 (Sullivan explaining that “[t]he technologies claimed in the patents-in-suit do not offer significant benefits over prior art,” and citing Chang Report ¶¶ 135-

201). Bio-Rad maintains that the Ismagilov patents are “fundamental” and “important” patents for conducting reactions in droplets. But the portions copied from *Quake* describe droplets that “are used as microreactors for chemical reactions (including biochemical reactions).” Ex. 3 at DTX-0386.0016. The content and extent of Ismagilov’s copying shows that, if the Ismagilov patents describe any patentable invention, they are limited to minor advances in the art. This evidence is designed to “show[] the jury the small differences between the invention and prior art,” and will “demonstrate[] that many of the benefits [patentee] attributed to the [claimed invention] were already present in the prior art.” *Exmark Mfg. Co. Inc. v. Briggs & Stratton Power Prod. Grp., LLC*, 879 F.3d 1332, 1351 (Fed. Cir. 2018) (finding abuse of discretion when district court excluded evidence of similarities between invention and prior art used to support a lower a royalty rate).

Bio-Rad will not be unfairly prejudiced by evidence of copying or introduction of the provisional. The provisional application and Dr. Ismagilov’s copying of *Quake* is relevant. The jury is entitled to consider this evidence, which does not unfairly prejudice Bio-Rad. *See, e.g., Carter v. Hewitt*, 617 F.2d 961, 972 (3d Cir. 1980) (Rule 403 “does not offer protection against evidence that is merely prejudicial, in the sense of being detrimental to a party’s case. Rather, the rule only protects against evidence that is unfairly prejudicial.”). Bio-Rad enjoys the presumption of validity and will be allowed to tell the jury that *Quake* was before the Patent Office when the Ismagilov patents were first examined. D.I. 378 at 2-3.

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